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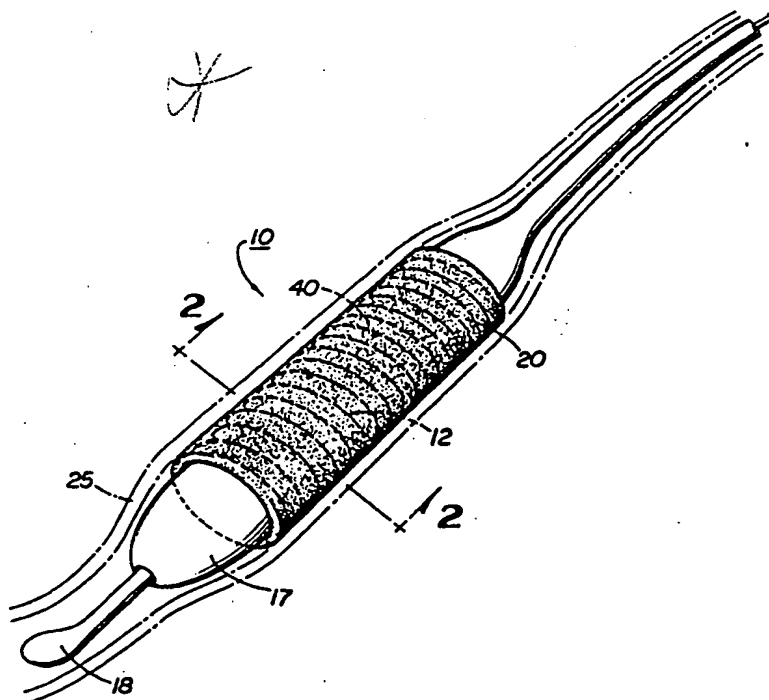
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(54) Title: ENDOVASCULAR SUPPORT DEVICE AND METHOD OF USE

(57) Abstract

This invention is an endovascular support device (10) adapted for local delivery of a therapeutic agent (50) for minimizing the rate of restenosis having a cylindrical support body (12) with an inside surface (14), an opposite outside surface (16), and at least one layer of pericardial tissue (20) covering at least a portion of at least a selected one of the inside surface (14), or the outside surface (16) of the cylindrical support body (12). At least one therapeutic agent (50) is disposed on a portion of the support device (10).



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## **ENDOVASCULAR SUPPORT DEVICE AND METHOD OF USE**

5

### **FIELD OF THE INVENTION**

The present invention relates to the field of endovascular support to maintain patency of narrowed vessels and facilitate repair of injured or degenerated vessels by  
10 implantation of a device within the target vessel. More specifically, the invention relates to acceptable biological coverings for an endovascular support device and the local delivery of a therapeutic substance into the vascular tissue, as a complementary treatment.

15

### **BACKGROUND OF THE INVENTION**

Partial and even complete blockage of the vascular system by the formation of an atherosclerotic plaque is a well known and frequent medical problem. Such blockages  
20 are often treated with percutaneous transluminal coronary angioplasty (PTCA), also known as balloon angioplasty, or by intravascular stent implantation. PTCA is an alternative to vascular bypass surgery, which includes a surgically exposing incision, and removing, replacing, or bypassing the defective blood vessel. Structures which have previously been used as intraluminal vascular grafts have included coiled stainless steel  
25 springs, and grafted stents made out of synthetic material (Dacron or PTFE). Examples

of such prior art devices may be found in U.S. Patent Nos. 5,306,286; 5,026,377; 5,019,085; 5,019,090; 4,913,141; 4,886,062; 4,733,665; and 4,503,569.

In balloon dilatation of vascular stenosis, or blockages, the balloon is inflated  
5 within the stenosed vessel, in order to shear and disrupt the wall component of the  
vessel to obtain an enlarged lumen. This may create a flap or tear at the intima or the  
media of the vessel wall. The intimal flap can fold down into the lumen and may  
occlude the vessel. Such occurrences contribute to the high incidence of restinosis  
which is prevalent. Currently, conventional balloon angioplasty is followed by roughly a  
10 30% to 50% incidence of restenosis.

Vascular prosthetic devices are often utilized in an effort to maintain vessel  
patency and prevent restinosis. However, vascular prosthetic devices or patches are  
often associated with increased thrombogenicity of the PTCA site due to the blood  
15 contacting the surfaces of the prosthetic device, and result in occlusion of the vesicle.  
Additionally, synthetic materials used in conventional endovascular prostheses tend to  
reject coverage by the patient's living tissue, i.e. endothelium, and have collecting  
surfaces that become thrombogenic sites. Previous biological materials suggested in the  
art for use in endovascular support have not provided a satisfactory ability to graft to the  
20 patient's tissues. Moreover, the body's own repair mechanisms can bring progressive  
stenotic occlusion due to neointimal fibrosis and hyperplasia. Additionally, an  
immunological response to foreign material can lead to increased inflammation in  
response to the prosthetic device.

Systemic therapy aimed at preventing coagulation, a thrombosis locally at the graft site, is often complicated at other sites and produces unwanted, even dangerous side effects. Likewise, systemic treatment with growth mediators or chemotherapeutic agents can produce a hyperplastic or hypoplastic response in tissue not specifically targeted. Existing stent devices, such as dip coated stents, providing locally delivered drugs do not satisfactorily promote grafting or integration of the stent into the patient's endothelium. See for example U.S. Patent Nos. 5,383,928 and 5,102,417.

Therefore, there exists a need in the art for a device and method for supporting endovascular vessels, which provides local therapy for repairing those blood vessels narrowed or occluded by disease, and which provides a biologically acceptable substrate for grafting to the patient. There is a need for such a device which includes providing local therapy resulting in high local concentrations of therapeutic drugs at the treatment site. The art has sought such an expandable intraluminal vascular support graft, and alternatively an independent arterial-vascular fistula, which prevents recurrence of stenosis, to be utilized to support or replace degenerated vein grafts, coronary arteries, and the peripheral arterial and venous system.

However, prior to the development of the present invention, there has been no expandable intraluminal graft comprised of a biological material which prevents recurrence of restenosis that can also be utilized to deliver drugs locally to the desired location.

## SUMMARY OF THE INVENTION

The present invention provides an endovascular support device adapted for local delivery of a therapeutic agent and for minimizing the rate of restinosis. The device has  
5 a cylindrical support body having an inside surface and an outside surface. The endovascular support device of the present invention also has at least one layer of pericardial tissue covering at least a portion of the inside surface or the outside surface of the cylindrical support body. The endovascular support device of the present invention is provided with a therapeutic agent disposed on a portion thereof.

10

## BRIEF DESCRIPTIONS OF THE DRAWINGS

Fig. 1 is a perspective view of the endovascular support device in accordance  
15 with one embodiment of the invention positioned on a balloon catheter delivery means inside a vesicle.

Fig. 2 is a cross section view of the endovascular support device taken along the  
plane defined by the line 2-2 in Fig. 1, and positioned within a vesicle.

20

Fig. 3 is a partial cut away view of the pericardial tissue of the endovascular support device with micropores disposed therethrough for delivery of a therapeutic agent.

Fig. 4 is a schematic side view of six (Figs. 4A-4F) alternative embodiments of the endovascular support device of the present invention.

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## DETAILED DESCRIPTION OF THE INVENTION

Referring to Figures 1-4, the present invention provides an endovascular support device 10 adapted for local delivery of a therapeutic agent 50 and for minimizing the rate of restinosis. The device 10 has a cylindrical support body 12 having an inside surface 14 and an opposite outside surface 16. The cylindrical support body 12 may be constructed of an expandable flexible wire coil or a tubular mesh of multiple coils or rings. Alternatively, the support body 12 may be constructed of a molded polymer, or similarly rigid substance, or a combination of the two.

15 An expandable support material can permit precise positioning and maintenance of the device 10 within a bodily vesicle 25, with the assistance of an angioplasty balloon 16, as shown in Figure 1. In common use, a guide wire 18 is inserted within the vesicle 25 to the point where endovascular support is desired. An angioplasty balloon 17, or other similar positioning device, carrying the endovascular support device 10 of the present invention, is moved through the vesicle 25 along the guide wire 18. At the 20 desired site, the balloon 17 is inflated and the device 10 is positioned against the walls of the vesicle. The angioplasty balloon 17 and guide wire 18 are then removed, leaving the device 10 in place to support the vesicle 25.

The invention contemplates that the endovascular support device 10 can be used within existing and grafted vesicles in a patient. The device 10 may be positioned within a vesicle for a variety of purposes, such as for structural support or to occlude an associated aneurysm, for example. The invention also contemplates that the device 10 can be used independently to provide a vascular replacement for ineffective vesicles, or as a separate fistula as for dialysis.

Referring to Figures 2 and 4, the endovascular support device 10 of the present invention also has at least one layer of pericardial tissue 20 covering at least a portion of the inside surface 14 or the outside surface 16 of the cylindrical support body 12. The pericardial tissue 20 provides a thin-walled membrane made of biological tissue to promote acceptance and fusion with the patient's blood vessel 25 tissue. The support device 10 surface may have an adjustable thickness by varying the number of tissue 20 layers. The pericardium may be chosen from any mammal, but is preferably of porcine, bovine, or human origin.

One skilled in the art will know how to prepare such a pericardial tissue 20 for a homograft or xenograft. For example, porcine pericardium may be retrieved from that surrounding the heart of a sacrificed pig. After shaving the excess fat, the tissue can be immersed in 0.2% glutaraldehyde, which creates permanent strengthening chemical cross-links. The porcine pericardium can then be immersed in porcine albumin solution. When the pericardium is wrapped on the support body 12, it may be adhered to the support body 12 with a biocompatible glue or by careful suturing. The pericardial tissue may be stored in a cold electrolyte solution until used.



Pericardial tissue provides a surprisingly effective biological endovascular support covering. This feature is due, at least in part, to the strength and elasticity of the tissue. The pericardium also has a very low degree of thrombogenicity and is biocompatible with graft recipients. Furthermore, the pericardium serves as an  
5 excellent drug delivery means, due to its porosity and high collagen content.

The endovascular support device 10 of the present invention can be provided with at least one therapeutic agent 40 disposed on a portion thereof. By "therapeutic agent" is meant any compound which has a desired pharmacologic effect. By "disposed  
10 on" is meant that the therapeutic agent 40 is in contact with at least a portion of the tissue or polymer, described below. For example, the therapeutic agent 40 can be soaked into the tissue or polymer over a period of time, or alternatively, can be injected into a reservoir or cavity created by layers of these materials. The invention  
contemplates that the device 40 may be made available either presoaked with a  
15 therapeutic agent, or provided such that a therapeutic agent is chosen for soaking or injection into the reservoir just prior to placement of the device 10 in the patient.

More specifically, the therapeutic agent 40 can be an anticoagulant, such as D-Phe-Pro-Arg chloromethyl ketone, an RGD peptide-containing compound, heparin, an  
20 antithrombin compound, a platelet receptor antagonist, an anti-thrombin antibody, an anti-platelet receptor antibody, aspirin, a prostaglandin inhibitor, a platelet inhibitor or a tick anti-platelet peptide. The therapeutic agent 40 can be a promoter of vascular cell growth, such as a growth factor stimulator, a growth factor receptor agonist, a transcriptional activator, and a translational promoter. Alternatively, the therapeutic

agent 40 can be an inhibitor of vascular cell growth, such as a growth factor inhibitor, a growth factor receptor antagonist, a transcriptional repressor, a translational repressor, an antisense DNA, an antisense RNA, a replication inhibitor, an inhibitory antibody, an antibody directed against growth factors, a bifunctional molecule consisting of a growth factor and a cytotoxin, or a bifunctional molecule consisting of an antibody and a cytotoxin.

The therapeutic agent 40 can be a cholesterol-lowering agent, a vasodilating agent, or other agents which interfere with endogenous vasoactive mechanisms.

10 Additionally, the therapeutic agent 40 can be a smooth muscle inhibitor, such as: an agent that modulates intracellular calcium binding proteins; a receptor blocker for contractile agonists; an inhibitor of the sodium/hydrogen antiporter; a protease inhibitor; a nitrovasodilator; a phosphodiesterase inhibitor; a phenothiazine; a growth factor receptor agonist; an anti-mitotic agent; an immunosuppressive agent; or a protein kinase

15 inhibitor.

The therapeutic agent 40 may be disposed on all or a portion of the pericardial tissue 20 to utilize the biological properties of the material to absorb different drugs and to release them slowly after deployment to the adjacent tissue. As seen in Figure 3, the

20 pericardial tissue 20 can have a plurality of micropores 22 that extend therethrough for more effective delivery of the therapeutic agent 40. The micropores 22 may also be made to extend only partially into one surface of the tissue 20, and not extend entirely therethrough, such that the therapeutic agent 40 can be directed to diffuse primarily in the direction of the micropores. For example, if only one layer of pericardial tissue 20 is

employed in the endovascular support device 10, the surface of the pericardial tissue 20 intended to face outward can have a plurality of micropores 22 disposed thereon for delivery of the therapeutic agent 50 primarily toward the adjacent walls of the blood vesicle 25, and not toward the interior of the vesicle 25. Micropores 22 can be made in  
5 the tissue 20 by a variety of means, including by laser incision.

Alternatively, the therapeutic agent 40 may be disposed on all or a portion of a polymer 50, which can be biodegradable and adapted for slow release of the therapeutic agent 40. A polymer 50 laden with one or more therapeutic agents 40 can be positioned  
10 on portion of the cylindrical support body 12, wrapped around a portion of the pericardial tissue 20, or imbedded between multiple layers of pericardial tissues 20.

Alternatively, the polymer 50 can be constructed so as to form the cylindrical support body 12 itself, then wrapped at least partially with at least one layer of pericardial tissue 20.

15

A biodegradable polymer 50 such as polylactide, polyanhydride, polyorthoester or polyglycolide, for example can be used. In addition to synthetic polymers, natural polymers can be used, such as amino acid polymers or polysaccharides. The polymer 50 is selected depending on the drug required, the polymer's 50 compatibility with a patient  
20 and the ultimate pharmacologic effect desired. For example, if the effect need only last a short period, a thin polymer 50 can be used with a limited amount of drug capable of diffusing from the polymer 50 into the arterial wall or lumen of the vesicle 25.

Alternatively, only the layer closest to the body fluid would contain the therapeutic

agent 40. Another alternative would be to use a polymer 50 which is biodegradable over a long period of time. Naturally, the opposite characteristics would be selected for a desired prolonged release.

5       The characteristics of the particular polymer 50 for these purposes is well known to the skilled artisan or can be determined by reference to standard references, e.g., *Biodegradable Polymers as Drug Delivery Systems*, R. Langer and M. Chasin, Eds., Marcel Dekker Inc., New York, NY, USA (1990); Engleberg and Kohn, "Physico-mechanical properties of degradable polymers used in medical applications: a  
10 comparative study," *Biomaterials* 12:292-304 (1991); *Controlled Release Delivery Systems*, T. J. Roseman and S. D. Mansdorf, Eds., Marcel Dekker Inc., New York, NY, USA (1983); and "Controlled Release Technology, Pharmaceutical Applications, ACS Symposium Series, Vol. 348, P. I. Lee and W. R. Good, Eds., American Chemical Society, Washington, D.C., USA (1987).

15       Generally, the polymer 50 has a therapeutic agent 40 release rate of between about .001  $\mu\text{g}/\text{cm}^2\text{-min}$  and about 100  $\mu\text{g}/\text{cm}^2\text{-min}$ , especially between about .01  $\mu\text{g}/\text{cm}^2\text{-min}$  and 10  $\mu\text{g}/\text{cm}^2\text{-min}$ . In addition, the polymer 50 generally has a thickness of between about .01 mm and 10 mm, especially between about .1 mm and 1 mm. As can  
20 be appreciated, the device 10 can be comprised of two or more different therapeutic agents 40 or two or more different polymers 50 to obtain a desired effect and release rate. In addition, the polymers 50 can have different solubilities or diffusion characteristics to accomplish non-uniform therapeutic agent 40 release.

Figures 4A-4F show a variety of combinations of the device 10 elements: the support body 12, pericardial tissue 20, and polymer 50, contemplated as different embodiments of the present invention. It is understood from the above description that the therapeutic agent 40 may be disposed on any or all of these elements. As discussed  
5 above, the therapeutic agent 40 can be, for example, soaked into the pericardial tissue or polymer, laminated on the pericardial tissue or polymer, or injected into a reservoir formed by these materials. Figure 4A shows one embodiment in which the support body 12 has a pericardial tissue 20 disposed on both the inside surface 14 and outside surface 16 thereof. Certainly, the invention contemplates that pericardium tissue 20 can  
10 be disposed on either surface alone. Figure 4B shows the support body 12 covered on the inside surface 14 by a layer of pericardial tissue 20, and covered on the outside surface 16 by a layer of polymer 50. Figure 4C shows an embodiment in which the support body 12 is covered on the inside surface 14 with a layer of polymer 50 which is in turn covered by a layer of pericardial tissue 20, and the outside surface 16 of the  
15 support body 12 is covered by a layer of polymer 50.

Figure 4D is the embodiment also shown in cross section in Figure 2. This embodiment has the support body 12 sandwiched on the inside surface 14 and the outside surface 16 between two layers of polymer 50, which is in turn sandwiched  
20 between two layers of pericardial tissue 20. Figure 4E presents an embodiment wherein the support body 12 is covered on the inside surface 14 by a layer of polymer 50, and on the outside surface 16 by a layer of pericardial tissue 20. Finally, Figure 4F shows an embodiment having a layer of polymer 50 disposed on the inside surface 14 and a layer

of polymer 50 disposed on the outside surface, which is also coated with a layer of pericardial tissue 20.

The present invention also provides methods of using the device 10 to support  
5 an endovascular vessel 25 and to locally deliver a therapeutic agent 40 to minimize the rate of restenosis. More particularly, the invention provides methods for treating or preventing a condition associated with coagulation, thrombus formation, fibrosis and restenosis at treated vascular sites.

10 Throughout this Specification, various publications are referenced. The disclosures of these publications in their entireties are hereby incorporated by reference into this application in order to more fully describe the state of the art to which the invention pertains.

15 The preceding examples are intended to illustrate, but not limit the invention. While they are typical of those that might be used, other procedures known to those skilled in the art may be alternatively employed. As used herein, "a" means one or more than one, depending upon the context.

## WHAT IS CLAIMED IS:

1. An endovascular support device adapted for local delivery of a therapeutic agent and for minimizing the rate of restenosis, comprising:
  - a. a cylindrical support body having an inside surface and an opposite outside surface;
  - b. at least one layer of pericardial tissue covering at least a portion of at least a selected one of said inside surface or said outside surface of said cylindrical support body; and,
  - c. a therapeutic agent disposed on a portion of said pericardial tissue, thereby adapting said endovascular support device for local delivery of the therapeutic agent and for minimizing the rate of restenosis.
2. The endovascular support device of claim 1, wherein said support body is comprised of material selected from the group consisting of a metal and a plastic polymer.
3. The endovascular support device of claim 1, further comprising at least one layer of a polymer on at least a portion of said cylindrical support body.
4. The endovascular support device of claim 3, wherein a second therapeutic agent is disposed on at least a portion of said polymer.
5. The endovascular support device of claim 1, wherein said pericardial tissue is

selected from the group consisting of porcine, bovine and human pericardial tissue.

6. The endovascular support device of claim 1, wherein the pericardial tissue has a plurality of micropores therethrough for delivery of said therapeutic agent.

7. The endovascular support device of claim 1, wherein a surface of the pericardial tissue has a plurality of micropores thereon for delivery of said therapeutic agent.

8. The endovascular support device of claim 1, wherein said therapeutic agent is disposed upon said pericardial tissue covering at least a portion of said inside surface of said cylindrical support body.

9. The endovascular support device of claim 1, wherein said therapeutic agent is an anticoagulant selected from the group consisting of D-Phe-Pro-Arg chloromethyl ketone, an RGD peptide-containing compound, heparin, an antithrombin compound, a platelet receptor antagonist, an anti-thrombin antibody, an anti-platelet receptor antibody, aspirin, a prostaglandin inhibitor, a platelet inhibitor and a tick anti-platelet peptide, and combinations thereof.

10. The endovascular support device of claim 1, wherein said therapeutic agent is a promoter of vascular cell growth selected from the group consisting of a growth factor stimulator, a growth factor receptor agonist, a transcriptional activator, and a translational promoter, and combinations thereof.



11. The endovascular support device of claim 1, wherein said therapeutic agent is an inhibitor of vascular cell growth selected from the group consisting of a growth factor inhibitor, a growth factor receptor antagonist, a transcriptional repressor, a translational repressor, an antisense DNA, an antisense RNA, a replication inhibitor, an inhibitory antibody, an antibody directed against growth factors, a bifunctional molecule consisting of a growth factor and a cytotoxin, and a bifunctional molecule consisting of an antibody and a cytotoxin, and combinations thereof.

12. The endovascular support device of claim 1, wherein said therapeutic agent is selected from the group consisting of a cholesterol-lowering agent, a vasodilating agent, and agents which interfere with endogenous vasoactive mechanisms, and combinations thereof.

13. The endovascular support device of claim 1, wherein said therapeutic agent is a smooth muscle inhibitor selected from the group consisting of an agent that modulates intracellular calcium binding proteins, a receptor blocker for contractile agonists, an inhibitor of the sodium/hydrogen antiporter, a protease inhibitor, a nitrovasodilator, a phosphodiesterase inhibitor, a phenothiazine, a growth factor receptor agonist, an anti-mitotic agent, an immunosuppressive agent, and a protein kinase inhibitor, and combinations thereof.

14. An endovascular support device adapted for local delivery of a therapeutic agent and for minimizing the rate of restenosis, comprising:

- a. a cylindrical support body having an inside surface and an opposite

- outside surface;
- b. at least one layer of pericardial tissue covering at least a first portion of at least a selected one of said inside surface or said outside surface of said cylindrical support body;
  - c. a polymer covering at least a second portion of at least a selected one of said inside surface or said outside surface of said cylindrical support body; and
  - d. a therapeutic agent disposed on said polymer, thereby adapting said endovascular support device for local delivery of the therapeutic agent and for minimizing the rate of restenosis.
15. The endovascular support device of claim 14, wherein at least a portion of said pericardial tissue is disposed on at least a portion of said polymer.
16. The endovascular support device of claim 14, wherein at least a portion of said pericardial tissue is disposed between at least a portion of said cylindrical support body and at least a portion of said polymer.
17. The endovascular support device of claim 14, wherein a second therapeutic agent is disposed on at least a portion of said pericardial tissue.
18. The endovascular support device of claim 14, wherein said pericardial tissue is selected from the group consisting of porcine, bovine and human pericardial tissue.
19. The endovascular support device of claim 14, wherein the pericardial tissue has a

plurality of micropores therethrough for delivery of said therapeutic agent.

20. The endovascular support device of claim 14, wherein a surface of the pericardial tissue has a plurality of micropores thereon for delivery of said therapeutic agent.

21. The endovascular support device of claim 14, wherein said therapeutic agent is an anticoagulant selected from the group consisting of D-Phe-Pro-Arg chloromethyl ketone, an RGD peptide-containing compound, heparin, an antithrombin compound, a platelet receptor antagonist, an anti-thrombin antibody, an anti-platelet receptor antibody, aspirin, a prostaglandin inhibitor, a platelet inhibitor and a tick anti-platelet peptide, and combinations thereof.

22. The endovascular support device of claim 14, wherein said therapeutic agent is a promoter of vascular cell growth selected from the group consisting of a growth factor stimulator, a growth factor receptor agonist, a transcriptional activator, and a translational promoter, and combinations thereof.

23. The endovascular support device of claim 14, wherein said therapeutic agent is an inhibitor of vascular cell growth selected from the group consisting of a growth factor inhibitor, a growth factor receptor antagonist, a transcriptional repressor, a translational repressor, an antisense DNA, an antisense RNA, a replication inhibitor, an inhibitory antibody, an antibody directed against growth factors, a bifunctional molecule consisting of a growth factor and a cytotoxin, and a bifunctional molecule consisting of

an antibody and a cytotoxin, and combinations thereof.

24. The endovascular support device of claim 14, wherein said therapeutic agent is selected from the group consisting of a cholesterol-lowering agent, a vasodilating agent, and agents which interfere with endogenous vasoactive mechanisms, and combinations thereof.

25. The endovascular support device of claim 14, wherein said therapeutic agent is a smooth muscle inhibitor selected from the group consisting of an agent that modulates intracellular calcium binding proteins, a receptor blocker for contractile agonists, an inhibitor of the sodium/hydrogen antiporter, a protease inhibitor, a nitrovasodilator, a phosphodiesterase inhibitor, a phenothiazine, a growth factor receptor agonist, an anti-mitotic agent, an immunosuppressive agent, and a protein kinase inhibitor, and combinations thereof.

26. An endovascular support device adapted for local delivery of a therapeutic agent and for minimizing the rate of restenosis, comprising:

- a. a cylindrical support body having an inside surface and an opposite outside surface;
- b. a first pericardial tissue covering at least a first portion of at least a selected one of said inside surface or said outside surface of said cylindrical support body; and
- c. a second pericardial tissue covering at least a second portion of at least a selected one of said inside surface or said outside surface of said cylindrical

support body; and

d. at least one therapeutic agent disposed in a reservoir between said first pericardial tissue and said second pericardial tissue, thereby adapting said endovascular support device for local delivery of the therapeutic agent and for minimizing the rate of restenosis.

27. The endovascular support device of claim 26, further comprising a polymer on at least a portion of said cylindrical support body.

28. The endovascular support device of claim 26, wherein a second therapeutic agent is disposed on at least a portion of said polymer.

29. The endovascular support device of claim 26, wherein said pericardial tissue is selected from the group consisting of porcine, bovine and human pericardial tissue.

30. The endovascular support device of claim 26, wherein the pericardial tissue has a plurality of micropores therethrough for delivery of said therapeutic agent.

31. The endovascular support device of claim 26, wherein a surface of the pericardial tissue has a plurality of micropores thereon for delivery of said therapeutic agent.

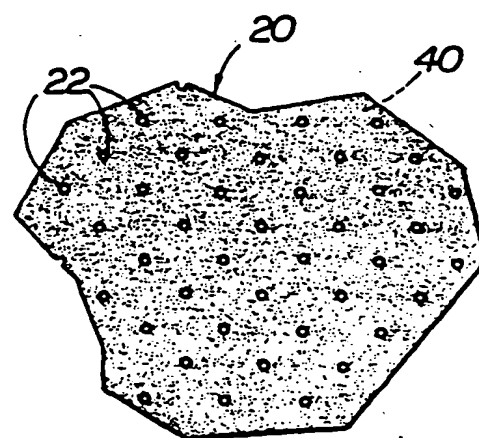
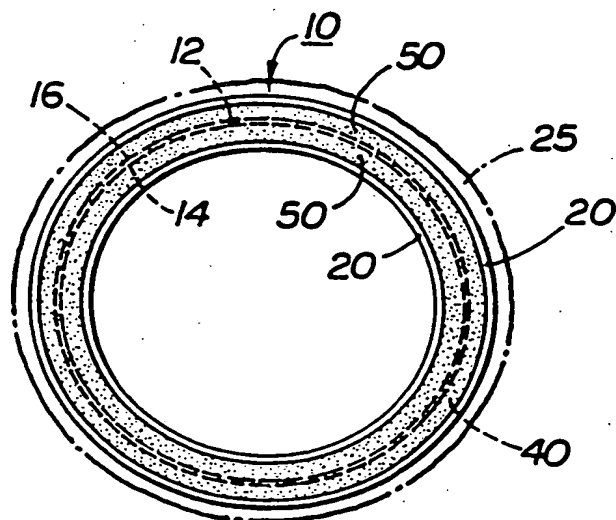
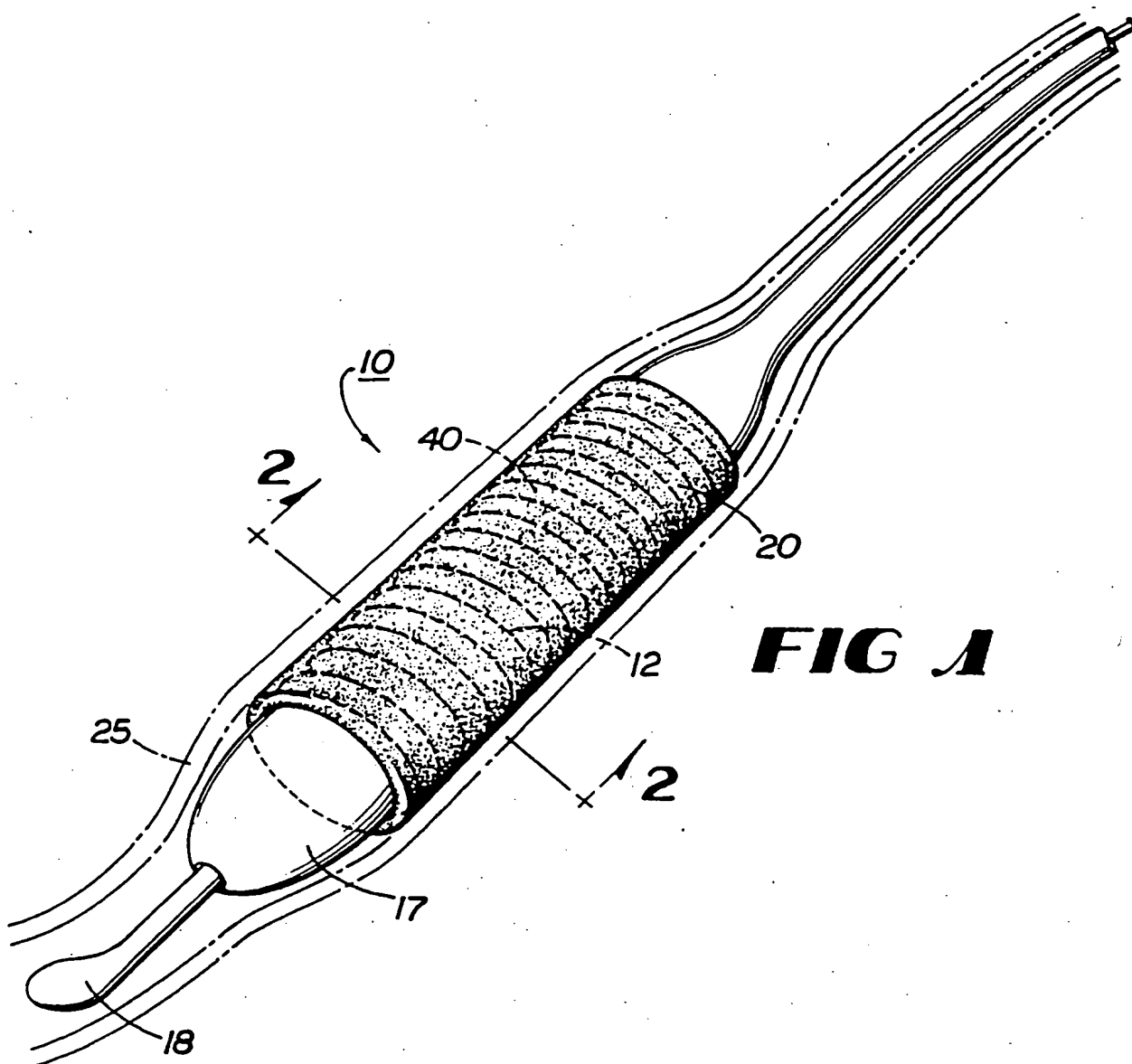
32. A method of supporting an endovascular vessel and locally delivering a therapeutic agent and minimizing the rate of restenosis, comprising inserting in the

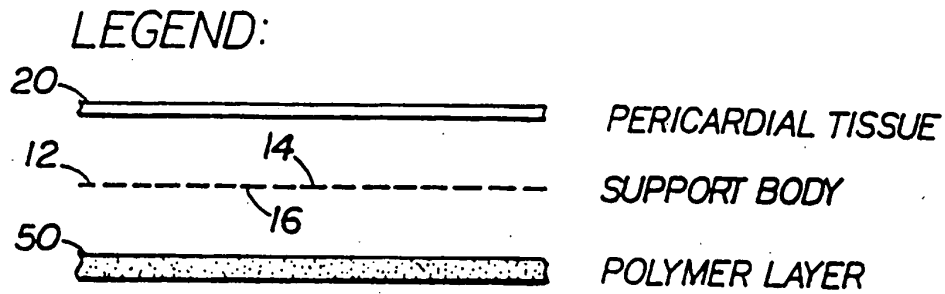
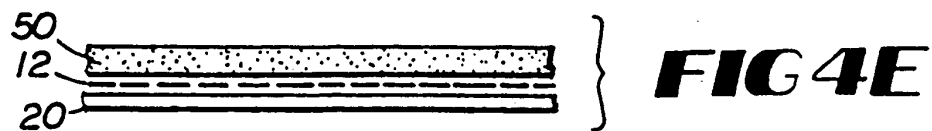
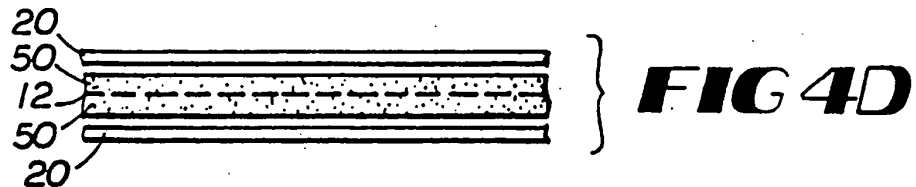
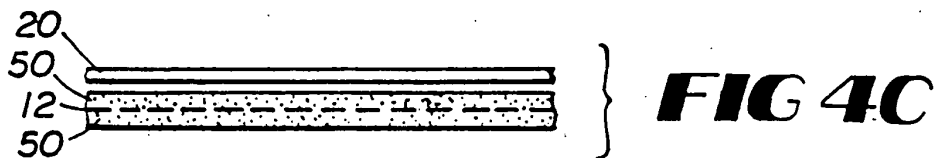
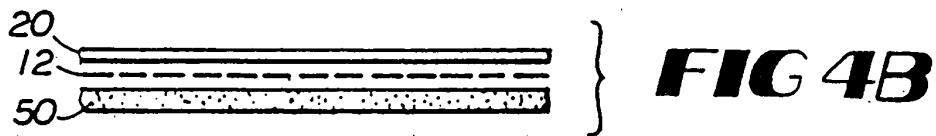
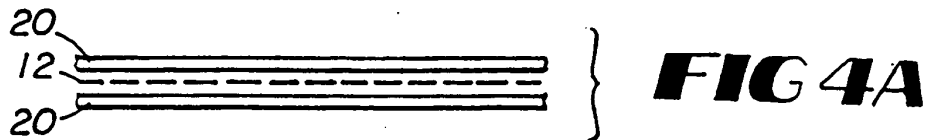
vessel an endovascular support device comprising:

- a. a cylindrical support body having an inside surface and an opposite outside surface;
- b. at least one layer of pericardial tissue covering at least a portion of at least a selected one of said inside surface or said outside surface of said cylindrical support body; and,
- c. a therapeutic agent disposed on at least a portion of said pericardial tissue, thereby supporting the endovascular vessel and locally delivering the therapeutic agent and minimizing the rate of restenosis.

33. A method of replacing a vascular vessel and locally delivering a therapeutic agent and minimizing the rate of restenosis, comprising replacing the vessel with an endovascular support device comprising:

- a. a cylindrical support body having an inside surface and an opposite outside surface;
- b. at least one layer of pericardial tissue covering at least a portion of at least a selected one of said inside surface or said outside surface of said cylindrical support body; and,
- c. a therapeutic agent disposed on at least a portion of said pericardial tissue, thereby replacing the endovascular vessel and locally delivering the therapeutic agent and minimizing the rate of restenosis.



**FIG 4**



# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US96/13907

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A61F 2/04, 06, 24, 54  
US CL : 424/423; 600/36; 623/1, 2, 11, 12, 66  
According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/423; 600/36; 623/1, 2, 11, 12, 66

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
APS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US, A, 5,383,927 (De GOICOECHIA ET AL.) 24 January 1995, see column 6 lines 4-20, column 7 lines 18-65, and Fig. 1B.	1-33
Y	US, A, 4,729,139 (NASHEF) 08 March 1988, see column 2 lines 38-62.	1-33
Y	US, A, 5,263,992 (GUIRE) 23 November 1993, see column 4 lines 24-50.	4, 17, 28
Y	US, A, 5,399,352 (HANSON) 21 March 1995, see column 5 line 59 to column 6 line 9, and Figs. 1, 2, 5 and 7.	9-13, 21-25, 32, 33

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

Special categories of cited documents:	
*A* document defining the general state of the art which is not considered to be part of particular relevance	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*E* earlier document published on or after the international filing date	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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*O* document referring to an oral disclosure, use, exhibition or other means	*Z* document member of the same patent family
*P* document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

04 OCTOBER 1996

Date of mailing of the international search report

24 OCT 1996

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# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US96/20868

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 4,666,442 A (ARRU et al) 19 May 1987, tissue sheet (11), and frame (2).	1-9, 20-22, 24, 25, 27, 31, 32, 34, 35, 37, 43-45 ----- 23, 33, 46

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